REMARKS

Claims 1-18 are pending in the application. Claims 1, 3, 4 and 7 have been amended. Claims 2, and 5 are held withdrawn. Claims 8-18 are cancelled. Support for the amended claims 1, 3, 4, and 7 can be found, for example, in paragraphs [122], [127], [130], [131], [311], and [315]. Support for new claims 19-22 can be found, for example, in paragraphs [49], [62], and in the table on page 34.

Applicants respectfully assert that no new matter has been introduced.

Claim objections

In the Office Action, the Examiner advises that should claims 61 and/or 62 be allowed, claims 63 and/or 64 will be objected to under 37 CFR 1.75 as being substantial duplicates. Applicants have cancelled claims 63 and 64, rendering this potential objection moot.

35 U.S.C. 112

In the Office action, the Examiner rejected claims 7-12 under 35 U.S.C. 112 alleging that the claims are indefinite. Applicants have amended claim 7 and withdrawn dependent claims therefrom, rendering the rejection moot. Accordingly, Applicants request withdrawal of the rejection.

35 U.S.C. 101

In the Office action, the Examiner rejected claims 7-12 under 35 U.S.C. 101 alleging that the claim is not a proper process claim, because of an improper definition of process. Applicants have amended claim 7 and withdrawn dependent claims therefrom, rendering the rejection moot. Accordingly, Applicants request withdrawal of the rejection.

35 U.S.C. 102(b)

In the Office action, the Examiner rejected Claims 13-18 under 35 U.S.C. 102(b) as allegedly being anticipated by Aoki et al. US 5,470,578. Applicants maintain that the compounds disclosed by Aoki do not anticipate, nor render obvious, the compounds claimed for use in the subject application, because Aoki describes a single phospholipid conjugated via a spacer to a terminal part of a GAG, while in the subject Application, the phospholipid is

directly conjugated at multiple sites of the GAG. Further, Aoki also does not describe the claimed use of the compounds of the present invention, that of treating sepsis. Thus, neither the compounds nor the uses of Aoki are applicable to the instant invention.

Applicants have cancelled claims 13-18 to expedite prosecution, rendering the rejection moot. Accordingly, Applicants request withdrawal of the rejection.

35 U.S.C. 103(a)

In the Office Action, the Examiner has rejected Claims 1-18 under 35 U.S.C. 103(a) as allegedly being obvious in view of the combined teaching of Yedgar et al., US 5,064,817, Chaikof et al., US 6,171,614, and Aoki et al., US 5,470,578, further in view of Pruzanski et al., US 6,043,231, Sorgente et al., US 6,162,787, and Falk et al. US 6,022,866. Applicants disagree.

The claimed invention is directed to a method of treating a subject suffering from sepsis, comprising the step of administering to a subject a lipid or phospholipid moiety bonded to a glycosaminoglycan (GAG).

The Examiner alleged that Yedgar et al. disclose compounds including distearoyl phosphatidylethanolamines covalently bonded through their amino groups to carrier moieties which may include polysaccharides, which are PLA2 inhibitors that may be effective in treating hyper-secretory disease states.

The compounds that Yedgar discloses are not the claimed compounds of the present invention. Yedgar's compounds comprise a lipid or phospholipid conjugated to an inert carrier, while the compounds of the present invention comprise a lipid or phospholipid conjugated to a GAG, which is biologically active. Yedgar also does not describe the claimed use of the compounds of the present invention. Yedgar claims uses in treating hyper-secretory disease states, while the present invention claims use in treating sepsis. Thus, neither the compounds nor the uses of Yedgar are applicable to the instant invention.

The Examiner alleged that Chaikof et al. disclose targeting of therapeutic agents using glycophospholipids, which may themselves be therapeutic, including chondroitin sulfate. The compounds described in Chaikof comprise a lipid or phospholipid conjugated to a GAG via an ether bond, while the compounds of the present invention comprise a lipid or phospholipid conjugated to a GAG via an amide or ester bond. Thus, the compounds of Chaikof are not

equivalent to the compounds claimed for use in the subject Application. Moreover, Chaikof does not describe treating sepsis. Thus, neither the compounds nor the uses of Chaikof are applicable to the instant invention. Further, there is no motivation to combine Chaikof with Yedgar, since such combination neither arrives at the compounds of this invention, nor the claimed use. While Yedgar describes conjugating a lipid or phospholipid to an inert carrier, it does not describe treating sepsis, and while Chaikof suggests that a GAG may be therapeutic, Chaikof as well does not describe treating sepsis. Thus, Chaikof neither describes the compounds of the present invention nor the use of any compound in treating sepsis.

The Examiner alleged that Aoki et al. discloses antirheumatic compositions generically overlapping applicants' with anticipating examples. Aoki et al. does not describe the compounds claimed for treating sepsis in the subject application, since the compounds in Aoki comprise phospholipids terminally conjugated to a GAG via a carrier molecule, typically a single saccharide unit. In the subject Application, the phospholipid is directly conjugated to the GAG, at multiple sites on the molecule. Further, Aoki does not describe the claimed uses of the present invention, that of treating sepsis. Thus, neither the compounds nor the uses of Aoki are applicable to the instant invention. It would not be obvious to arrive at the subject Application by combining Aoki with Chaikof and Yedgar, since such combination does not arrive at the compounds or claimed use in the subject Application, therefore, Applicants maintain that Yedgar, Chaikof, Aoki, or a combination thereof do not render the claimed invention obvious.

Falk et al. demonstrated that hyaluronic acid is useful in treating restenosis. Falk however, describes use of an unconjugated GAG, while the compounds of the present invention comprise a lipid or phospholipid conjugated to a GAG. Further, Falk does not describe use of the compounds for treating sepsis, but rather for preventing restenosis, a condition unrelated to sepsis. Moreover, **unconjugated GAGs are not as effective as conjugated GAGs**, whose use is claimed in the subject Application (Figs. 1.2, 1.3, 7.3, 8.7, 8.8, 12.1, and 15.1 and Table 5.3). Thus, neither the compounds nor the uses of Falk are applicable to the instant invention. There would be no motivation to combine Falk with Aoki, Chaikof and/or Yedgar, since neither the uses nor the compounds of the instant invention are taught by the combination. Moreover, since Falk describes unconjugated GAGs, which Applicants show are not as useful in the treatment proposed in the instant invention, Falk is not an appropriate reference in this context.

The Examiner alleged that Sorgente et al. describe the use of chondroitin sulfate as an anti-inflammatory. Sorgente describes combined application of collagen Type II and an unconjugated GAG, while Applicants claim use of a lipid or phospholipid conjugated to a GAG. Sorgente claims use of the combined therapy in treating arthritis, while Applicants claim use in treating sepsis. Thus, neither the compounds nor the uses of Sorgente are applicable to the instant invention. There would be no motivation to combine Sorgente with Falk, Aoki, Chaikof and/or Yedgar, for reasons similar to those disclosed for Falk et al., since Applicants have shown that unconjugated GAGs are not as effective as the claimed compounds in treating sepsis. Thus, none of the references cited render the claims of the subject application, the use of a lipid or phospholipid moiety bonded to a GAG for treating sepsis.

Pruzanski et al. describe use of a single modified tetracycline in treating sepsis. While Pruzanski describes treating sepsis, the compound is not related to the compounds claimed for use in the subject Application. There would be no motivation to combine Pruzanski with Sorgente, Falk, Aoki, Chaikof and/or Yedgar, since none of the latter references describe the claimed compounds, nor do they demonstrate comparable activity of a tetracycline with the claimed compounds, and thus their combined descriptions do not lead the skilled artisan to the use of a lipid or phospholipid moiety bonded to a GAG for treating sepsis.

Applicants maintain that none of the references, alone or in combination render the claims of the subject Application obvious, that of the use of lipid or phospholipid conjugated GAGs provide in treating sepsis, and accordingly, Applicants respectfully request withdrawal of the rejection.

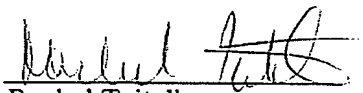
4. 35 U.S.C. 101 Double Patenting

The Examiner provisionally rejected Claims 13-18 allegedly under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application No. 09756,765 (Attorney Reference No: P-2507-US). Applicants have cancelled claims 13-18, rendering the rejection moot. Accordingly, Applicants request withdrawal of the rejection.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

No fee is deemed necessary for filing this Amendment. However, if any fee is required, the undersigned attorney hereby authorizes the United States Patent and Trademark Office to charge deposit account No. 50-3355.

Respectfully submitted,



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